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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/762,959 | 01/21/2004 | David A. Griffith | PC25408A | 7298 |

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
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| EXAMINER | |
|---|---|
| MOORE, SUSANNA | |
| **ART UNIT** | **PAPER NUMBER** |
| 1624 | |

DATE MAILED: 09/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/762,959 | GRIFFITH, DAVID A. | |
| | Examiner | Art Unit | |
| | Susanna Moore | 1624 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-99,101,103-111,113,115 and 117-127* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-99,101,103-111,113,115 and 117-127* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/7,8/2,8/6/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Arguments*

Applicant's arguments, filed 7/7/06, with respect to the Non-Final Office action, mailed 4/19/06 have been fully considered. Claims 100,102,112,114 and 116 were cancelled by Applicant.

### *Specification*

Regarding the objection to the title, the new title overcomes the objection.

### *Claim Rejections - 35 USC § 112*

As for points (I-II) under the 112 Rejections, the rejections have been withdrawn. The (III-IV) points under the 112 Rejection heading are maintained.

Claims 1-99,101,103-111,113,115 and 117-127 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for other forms, does not reasonably provide enablement for solvates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are drawn to solvates. But the numerous examples presented all failed to produce a solvate. These cannot be simply willed into existence. As was stated in *Morton*

*International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here: there is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

Applicant argues that the process of making solvates is routine in the art and there is no requirement to provide any working examples. Both parts of the previous statement are true, but not one of Applicants many compounds were recovered as a solvate. It appears that Applicants compounds do not form solvates, and thus, do not meet the enablement requirement. If Applicants disagree, they are asked to explain how solvates will be prepared if they do not occur naturally.

Claims 99,101,103-111,113,115 and 117-122 are rejected under 35 U.S.C. 112, first paragraph, because the Specification, while being enabling for blocking the acute psychological and physiological effects of smoked marijuana and for treating obesity, does not reasonably provide enablement for treating Parkinson's disease, dementia, or any of the other specifically listed diseases whose treatment is claimed. As for the references cited by Applicant, only those references, which represent the state of the art at the time Applicants filed will be acknowledged in the office action.

The first set of diseases mentioned in the table are weight loss, obesity and bulimia. The Examiner already acknowledged the enablement for obesity.

The second set of diseases found in the table are depression and atypical depression but Applicant did not provide state of the art references prior to the filing date.

The third set of diseases listed in the table is bipolar disorders, psychoses and schizophrenia. The reference by Poncelet et. al. (1999) addresses whether a drug, SR 141716, could overcome the stimulus affects of cocaine, d-amphetamine, morphine and WIN 55212-2, known biogenic amine reuptake blockers in the synapse. These compounds are known to cause schizophrenic-type behaviour. The reference goes on to mention a cannabinoid "hypothesis" proposed by Emrich et. al., the first page, right-hand column, third paragraph, who believed cognitive dysfunction could be associated with dysregulation of an endogenous cannabinoid system. This is only a "hypothesis." Furthermore, Poncelet states the uncertainty of the role of the CB1 antagonist as playing a role in synaptic regulation, which is the basis of the whole paper. See the first page, right-hand column, bottom of second paragraph, "Although current data coverage to suggest that such systems play a major role in synaptic regulation..., little is known about their potential involvement in pathopsychological conditions." Finally, the reference concludes with, "The antagonistic activity of SR 141716 against the cognition disrupting or reward enhancing properties of drugs, such as morphine, amphetamine, cocaine known to provoke or exacerbate schizophrenic symptomatology suggests that blockade of CB1 receptors could have beneficial effects on this pathology and in particular on cognitive dysfunction."

"Could" or "suggests" are not the standards for enablement of disease treatment claims. It only raises this as a possibility.

The fourth set of diseases mentioned in the table is behavioral additions, suppression or reward-related behaviors. The reference by Mas-Nieto (2001) addresses whether SR 141716A was able to overcome the reward affects of morphine to assist with the withdrawal behavior. The fourth paragraph of the abstract states, "...this study supports the reported interaction between the endogenous cannabinoid and opioid systems, and suggests that SR 141716A warrants further investigations for a possible use in opioid addiction." Chaperon et. al. (1998) states on page 1, left-hand column, bottom of abstract, "...a cannabinoid link may be involved in the neurobiological events, allowing the perception of the rewarding value of various kinds of reinforcers...given alone SR 141716 supported neither CPP nor CPA." Sanudo-Pena (1997) recites in the last paragraph of the abstract, "These results suggest that endogenous cannabinoids serve normally to suppress reward or to induce aversion," addressing the effects of SR 141716A in rats. Finally, Mansbach et. al. (1996) states, "These results suggest SR is an effective antagonist of the psychoactive effects of cannabinoids." The terms "suggest," "may be" or "further investigations" are not the standard for enablement of disease treatment claims. Furthermore, the Examiner would like to point out the references provide structurally unrelated compounds. The four references provided by Applicant address the drug SR 141716A, N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2, 4-dichlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide, not Applicants pyrazolopyrimidine compounds.

The next disease, alcoholism, is addressed by Mechoulam et. al. (2003). The last paragraph on page 268 recites, "Thus, the authors suggest that there is a rationale for the use of CB1 receptor antagonists in the treatment of alcohol addiction." Not one statement in the whole reference states a CB1 antagonist has been used to treat alcoholism.

The next method of treatment claimed on the list is tobacco abuse. Cohen et. al. (2002) recites in the last sentence of the abstract, "Thus, SR 141716 may be effective in reduction of alcohol consumption, as previously suggested, and as an aid for smoking cessation." This implies that such uses were not art-recognized in 2002.

The next method of treatment, dementia, is addressed by Wolf et.al. (2003). The last sentence in the abstract states, "These results suggest that a cannabinoid CB1 receptor antagonist can improve consolidation processes and thus may be useful in treating memory disorders." The terms "suggest" or "may be" are not the standard for enablement of disease treatment claims. Moreover, the reference does not provide a CB1 antagonist in 2003, which was used to treat dementia. Note further that dementia involves more than memory disorders, and that most memory disorders are not a form of dementia.

The reference for attention deficit disorder (ADD) does not meet the date requirement. To date, there are no CB1 antagonists used to treat ADD, only drugs that affect biogenic amine neurotransmission.

Parkinson's disease, addressed by DiMarzo et. al. (2002), on page 1437, right-hand column, "Overactivation of the endocannabinoid system in the globus pallidus may play a part in the generation of parkinsonian symptoms." The authors "...suggest that endocannabinoids provide a neurochemical substrate for the interactions between neurotransmitter systems..." The Ferrer et. al. (2003) reference, addresses dyskinesias, a disabling motor complication which develops within 10 years in patients being treated with levadopa (l-dopa). The reference refers to this as an elusive effect of l-dopa on the endocannabinoid system. To date, there are no CB1 antagonists used to treat Parkinson's disease patients or dyskinesias. Note that Parkinson's disease itself is not treatable; current therapies are directed only to symptom alleviation.

The reference for inflammation does not meet the date requirement. Furthermore, inflammation is an umbrella term for the many types of inflammatory diseases. Some examples of inflammatory diseases are as followed, but not limited to: allergies, appendicitis, arteritis, arthritis, asthma, blepharitis, bronchiolitis, bronchitis, bursitis, cervicitis, cholangitis, cholecystitis, chorioamnionitis, colitis, conjunctivitis, cystitis, dacryoadenitis, dermatitis, dermatomyositis, encephalitis, endocarditis, endometritis, enteritis, enterocolitis, epicondylitis, epididymitis, fasciitis, fibrositis, gastritis, gastroenteritis, gingivitis, hepatitis, hidradentitis supparativa, ileitis, immune reconstitution inflammatory syndrome (IRIS), laryngitis, mastitis, meningitis, myelitis, myocarditis, myositis, nephritis, omphalitis, oophoritis, orchitis, osteitis, otitis, pancreatitis, parotitis, pelvic inflammatory disease (PID), pericarditis, peritonitis, pharynx, pleuritis, phlebitis, pneumonitis, protitis, prostatitis, rhinitis, salpingitis, sinusitis, stomatitis, synovitis, tendonitis, tonsillitis, uveitis, vaginitis, vasculitis and vulvitis.

These are all different diseases in different parts of the body, which require different treatment, e.g. an appendicitis requires the removal of the appendix, while a pelvic inflammatory disease requires treatment with an antibiotic.

"Gastrointestinal (GI) disorders" is an umbrella term for the many types of GI diseases. Gastrointestinal disorders can be defined as any disease or disorder associated with the GI tract, which include the mouth, esophagus, stomach, intestines, rectum and anus. Other organs, such as the spleen, bile ducts, gall bladder, liver and pancreas, can also be a cause of gastrointestinal disorders. As recited, the scope of the claim can include, but is not limited to, tooth decay, periodontal disease, abscesses, canker sores, cold sores, oral cancer, gastroesophageal reflux disease, dysphagia, esophagus cancer, circopharyngeal incoordination, achalasia, diverticula, burning mouth syndrome, pancreas cancer, Crohn's disease, colon polyps, diverticular disease, intestinal parasites, salivary gland disease, sialhorria, dentigerous cyst, glossitis, benign migratory, Ludwig's Angina, Melkerson-Rosenthal Syndrome, xerostamia, Pierre-Robin Syndrome, diabetes, lactose intolerance, bruxism,ulcerative colitis, cystic fibrosis, pernicious anemia, tropical sprue, cirrhosis, Bassen-Kornzweig syndrome, pancreatitis, Shwachman-Diamond syndrome, anal cancer, acute pancreatitis, anal fissure, anal fistula, colorectal cancer, hemorrhoids, perirectal abscess, proctitis, rectal prolapse, functional constipation, liver cancer, diarrhea, ankyloglossia, Irritable Bowel Syndrome, functional dyspepsia, peptic ulcer, intussusception, Coeliac disease, Whipple's disease, lymphoma, incontinence, chronic pancreatitis, Hirschsprung's disease, infant regurgitation, biliary disorder, hemochromatosis, Wilson disease, tyrosinemia, alpha 1 antitrypsin defiency, glycogen storage disease, primary

sclerosing cholangitis, hepatitis A, hepatitis B, hepatitis C, Reyes's syndrome.

The reference by Croci et. al. (2003), provided by Applicant, addresses the state of the art of CB1 antagonists for the treatment of GI diseases. The reference states on page 120, right-hand column, last paragraph, "The effects of SR 141716 on the immune system should be further investigated, using these and other established in vivo and in vitro models of inflammation and immunity...". On page 121, left-hand column, Croci goes on to say, "Thus, SR 141716 and generally cannabinoid CB1 receptor antagonists could be potential new anti-inflammatory therapeutic agents to be used in acute and chronic diseases...". The phrases "should be further investigated" or "could be potential" are not the standards for enablement of disease treatment claims, and indeed, to show that enablement was not achieved.

The reference for type II diabetes does not meet the date requirement and thus does not represent the state of the art prior to the filing date.

The scope of the claims involves the millions of compounds of claim 1 as well as the broad scope embraced by the many diseases found in claim 99.

Claims 98, 103, 109, 115 and 120 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "analog thereof" is indefinite. What are these analogs of dehydroepiandrosterone?

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susanna Moore whose telephone number is (571) 272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SM

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